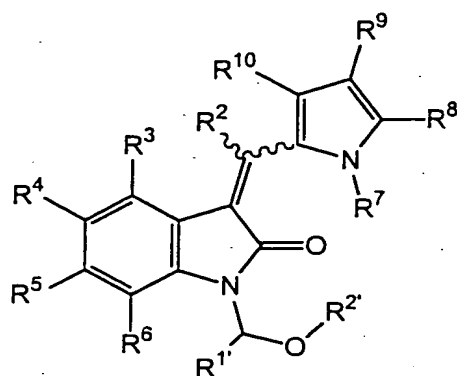
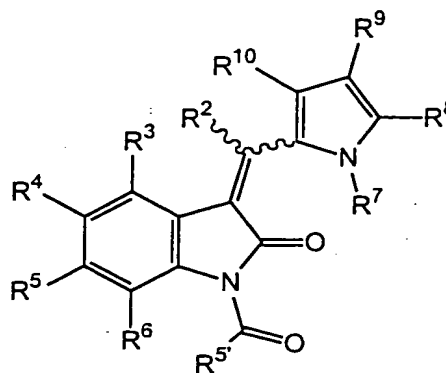


## WHAT IS CLAIMED IS:

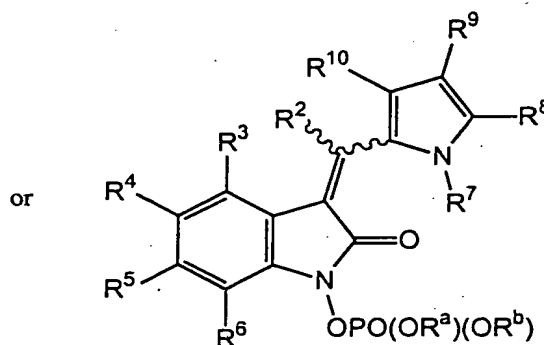
1. A compound of the formula I, III, or IV:



I



III



IV

5 wherein:

$R^2$  is hydrogen;

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and  $-NR^{11}R^{12}$  where  $R^{11}$  and  $R^{12}$  are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, acetyl, sulfonyl, and trifluoromethanesulfonyl, or  $R^{11}$  and  $R^{12}$ , together with the nitrogen atom to

which they are attached, combine to form a five- or six-membered heteroalicyclic ring provided that at least two of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; or

$R^3$  and  $R^4$ ,  $R^4$  and  $R^5$ , or  $R^5$  and  $R^6$  combine to form a six-membered aryl ring, a methylenedioxy or an ethylenedioxy group;

5  $R^7$  is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;

10  $R^8$ ,  $R^9$  and  $R^{10}$  are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino,  $-(alk)_1Z$  (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is  
15 hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl) and  $-NR^{11}R^{12}$  wherein  $R^{11}$  and  $R^{12}$  are as defined above;

$R^{1'}$  is hydrogen or alkyl;

$R^{2'}$  is hydrogen, alkyl, aralkyl, acyl, or  $-P(O)(OR)(OR')$ ;

20  $R^{5'}$  is alkyl;

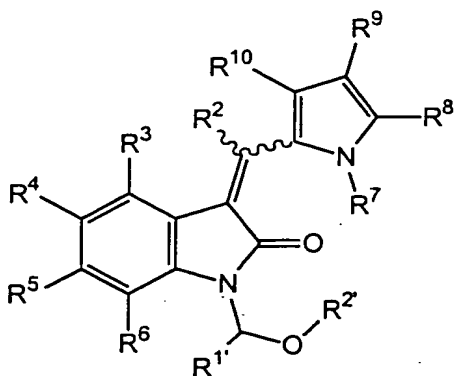
$R$  and  $R'$  are independently selected from the group consisting of hydrogen, alkyl, aralkyl and aryl;

$R^a$  and  $R^b$  are independently selected from hydrogen or alkyl; or  
a pharmaceutically acceptable salt thereof.

25

2. A compound of formula I:

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wherein:

$R^2$  is hydrogen;

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from the group consisting of  
 5 hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl,  
 heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl,  
 S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-  
 carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-  
 thiocarbamyl, N-thiocarbamyl, amino and  $-NR^{11}R^{12}$  where  $R^{11}$  and  $R^{12}$  are independently  
 10 selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, acetyl,  
 sulfonyl, and trifluoromethanesulfonyl, or  $R^{11}$  and  $R^{12}$ , together with the nitrogen atom to  
 which they are attached, combine to form a five- or six-membered heteroalicyclic ring  
 provided that at least two of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; or

$R^3$  and  $R^4$ ,  $R^4$  and  $R^5$ , or  $R^5$  and  $R^6$  combine to form a six-membered aryl ring, a  
 15 methylenedioxy or an ethylenedioxy group;

$R^7$  is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl,  
 alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-  
 amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-  
 sulfonyl;

20  $R^8$ ,  $R^9$  and  $R^{10}$  are independently selected from the group consisting of hydrogen,  
 alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy,  
 alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-  
 sulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, O-carbamyl, N-  
 carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino,  $-(alk)_1Z$   
 25 (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is  
 hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido,

sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl) and  $-NR^{11}R^{12}$  wherein  $R^{11}$  and  $R^{12}$  are as defined above;

$R^{1'}$  is hydrogen or alkyl;

$R^{2'}$  is hydrogen, alkyl, aralkyl, acyl or  $-P(O)(OR)(OR')$  where  $R$  and  $R'$  are  
5 independently selected from the group consisting of hydrogen, alkyl, aralkyl or aryl; or a pharmaceutically acceptable salt thereof.

3. The compound of Claim 2, wherein  $R^{1'}$ ,  $R^{2'}$  and  $R^7$  are hydrogen.

10 4. The compound of Claim 3, wherein:

$R^3$  is hydrogen or lower unsubstituted alkyl;

$R^4$  is selected from the group consisting of hydrogen, halogen, aryl and S-sulfonamido;

$R^5$  is selected from the group consisting of hydrogen, lower alkyl, lower  
15 alkoxy, aryl, and heteroaryl; and

$R^6$  is hydrogen.

5. The compound of Claim 3, wherein:

$R^3$  is hydrogen;

20  $R^4$  is selected from the group consisting of hydrogen, chloro, fluoro, bromo and phenyl;

$R^5$  is selected from the group consisting of hydrogen, methyl, ethyl, methoxy, phenyl, and pyridyl.

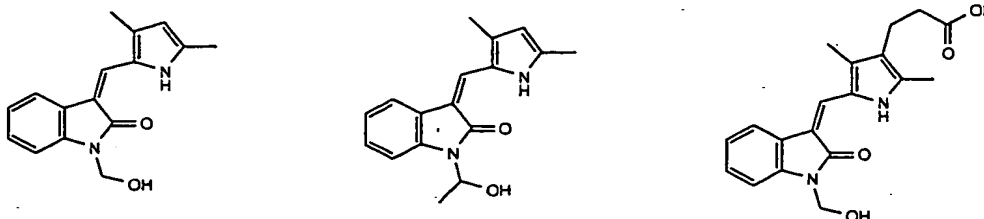
25 6. The compound of Claim 3, wherein:

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

$R^8$  and  $R^{10}$  are unsubstituted lower alkyl; and

$R^9$  is hydrogen, C-amido, or  $-(alk_1)Z$  (where  $alk_1$  is selected from the group  
30 consisting of alkyl, alkenyl or alkynyl and  $Z$  is hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl).

7. The compound of Claim 2, wherein the compound is selected from the group consisting of:



and

8. The compound of Claim 2, wherein:

$R^{2'}$  is  $-P(O)(OR)(OR')$ ; and

$R^7$  is hydrogen.

9. The compound of Claim 8, wherein:

$R^3$  is hydrogen or lower unsubstituted alkyl;

$R^4$  is selected from the group consisting of hydrogen, halogen, aryl and S-sulfonamido;

$R^5$  is selected from the group consisting of hydrogen, lower alkyl, lower alkoxy, aryl, and heteroaryl; and

$R^6$  is hydrogen.

10. The compound of Claim 8, wherein:

$R^3$  is hydrogen;

$R^4$  is selected from the group consisting of hydrogen, chloro, fluoro, bromo, phenyl, even more preferably hydrogen or fluoro;

$R^5$  is selected from the group consisting of hydrogen, methyl, ethyl, methoxy, phenyl, and pyridyl.

11. The compound of Claim 8, wherein:

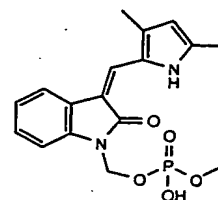
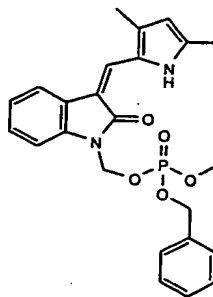
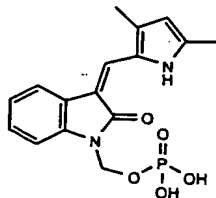
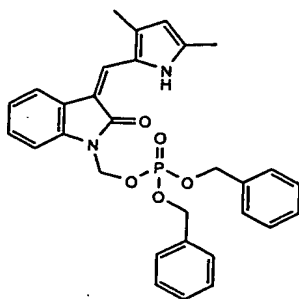
$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

$R^8$  and  $R^{10}$  are unsubstituted lower alkyl; and

$R^9$  is hydrogen, C-amido, or  $-(alk)_1Z$  (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is hydroxy, alkoxy, carboxy, nitro, cyano, amino,

guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl).

12. The compound of Claim 8, wherein the compound is selected from the group consisting of



and

13. The compound of Claim 2, wherein  $R^{2'}$  is acyl; and  $R^7$  is hydrogen.

14. The compound of Claim 13, wherein:

$R^3$  is hydrogen or lower unsubstituted alkyl;

$R^4$  is selected from the group consisting of hydrogen, halogen, aryl and S-sulfonamido;

$R^5$  is selected from the group consisting of hydrogen, lower alkyl, lower alkoxy, aryl, and

heteroaryl; and

$R^6$  is hydrogen.

15. The compound of Claim 13, wherein:

$R^3$  is hydrogen;

$R^4$  is selected from the group consisting of hydrogen, chloro, fluoro, bromo and phenyl;

$R^5$  is selected from the group consisting of hydrogen, methyl, ethyl, methoxy, phenyl, and pyridyl.

16. The compound of Claim 13, wherein:

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

$R^8$  and  $R^{10}$  are unsubstituted lower alkyl; and

5

and

wherein:

$R^2$  is hydrogen;  
 $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and  $-NR^{11}R^{12}$  where  $R^{11}$  and  $R^{12}$  are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, acetyl, sulfonyl, and trifluoromethanesulfonyl, or  $R^{11}$  and  $R^{12}$ , together with the nitrogen atom to which they are attached, combine to form a five- or six-membered heteroalicyclic ring provided that at least two of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; or  $R^3$  and  $R^4$ ,  $R^4$  and  $R^5$ , or  $R^5$  and  $R^6$  combine to form a six-membered aryl ring, a methylenedioxy or an ethylenedioxy group;  
 $R^7$  is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;  
 $R^8$ ,  $R^9$  and  $R^{10}$  are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino,  $-(alk)_1Z$  (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl) and  $-NR^{11}R^{12}$  wherein  $R^{11}$  and  $R^{12}$  are as defined above; and  
 $R^5$  is alkyl; or  
a pharmaceutically acceptable salt thereof.

20. The compound of Claim 19, wherein  $R^5$  is alkyl substituted with C-carboxy,  
 $-NR^{11}R^{12}$  or ammonium.



21. The compound of Claim 20, wherein:

$R^3$  is hydrogen or lower unsubstituted alkyl;

$R^4$  is selected from the group consisting of hydrogen, halogen, aryl and S-sulfonamido;

5  $R^5$  is selected from the group consisting of hydrogen, lower alkyl, lower alkoxy, aryl, and heteroaryl; and

$R^6$  is hydrogen.

22. The compound of Claim 20, wherein:

$R^3$  is hydrogen;

10  $R^4$  is selected from the group consisting of hydrogen, chloro, fluoro, bromo and phenyl;

$R^5$  is selected from the group consisting of hydrogen, methyl, ethyl, methoxy, phenyl, and pyridyl.

23. The compound of Claim 20, wherein:

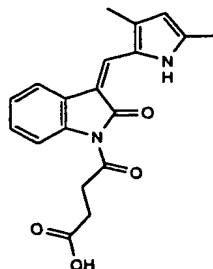
15  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

$R^8$  and  $R^{10}$  are unsubstituted lower alkyl; and

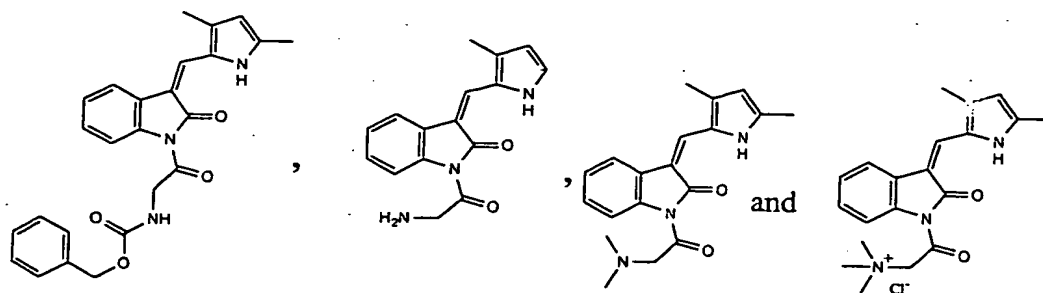
$R^9$  is hydrogen, C-amido, or  $-(alk_1)Z$  (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino,

20 piperazinyl or tetrazolyl).

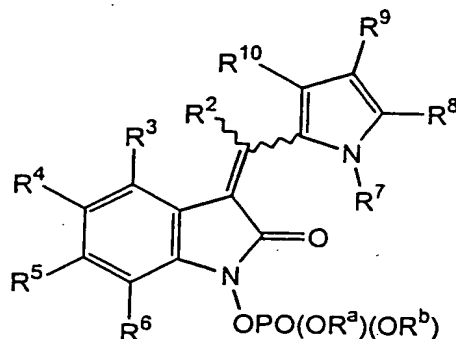
24. The compound of Claim 20, wherein the compound is:



25. The compound of Claim 20, wherein the compound is selected from the group consisting of:



26. A compound of formula IV:



wherein:

$R^2$  is hydrogen;

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and  $-NR^{11}R^{12}$  where  $R^{11}$  and  $R^{12}$  are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, acetyl, sulfonyl, and trifluoromethanesulfonyl, or  $R^{11}$  and  $R^{12}$ , together with the nitrogen atom to which they are attached, combine to form a five- or six-membered heteroalicyclic ring provided that at least two of  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; or  $R^3$  and  $R^4$ ,  $R^4$  and  $R^5$ , or  $R^5$  and  $R^6$  combine to form a six-membered aryl ring, a methylenedioxy or an ethylenedioxy group;

R<sup>7</sup> is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;

R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of hydrogen, alkyl,

5 trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino, -(alk)<sub>1</sub>Z

(where alk<sub>1</sub> is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is  
10 hydroxy, alkoxy, carboxy, nitro, cyano, amino, guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl) and -NR<sup>11</sup>R<sup>12</sup> wherein R<sup>11</sup> and R<sup>12</sup> are as defined above; and

R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen or alkyl; or  
a pharmaceutically acceptable salt thereof.

15

27. The compound of Claim 26, wherein R<sup>7</sup> is hydrogen.

28. The compound of Claim 27, wherein:

R<sup>3</sup> is hydrogen or lower unsubstituted alkyl;

20 R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, aryl and S-sulfonamido;

R<sup>5</sup> is selected from the group consisting of hydrogen, lower alkyl, lower alkoxy, aryl, and heteroaryl; and

R<sup>6</sup> is hydrogen.

25 29. The compound of Claim 27, wherein:

R<sup>3</sup> is hydrogen;

R<sup>4</sup> is selected from the group consisting of hydrogen, chloro, fluoro, bromo, phenyl, even more preferably hydrogen or fluoro;

R<sup>5</sup> is selected from the group consisting of hydrogen, methyl, ethyl, methoxy, phenyl, and  
30 pyridyl.

30. The compound of Claim 27, wherein:

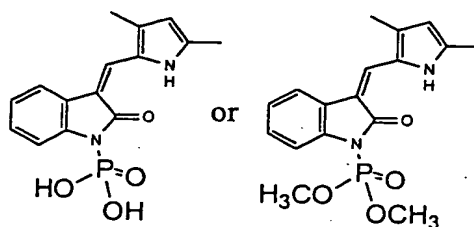
$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

$R^8$  and  $R^{10}$  are unsubstituted lower alkyl; and

$R^9$  is hydrogen, C-amido, or  $-(alk)_1Z$  (where  $alk_1$  is selected from the group consisting of alkyl, alkenyl or alkynyl and Z is hydroxy, alkoxy, carboxy, nitro, cyano, amino,

5 guanidino, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphonate, morpholino, piperazinyl or tetrazolyl).

31. The compound of Claim 27, wherein the compound is:



10

32. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

33. A pharmaceutical composition comprising a compound of any one of  
15 Claims 2-18 and a pharmaceutically acceptable carrier.

34. A pharmaceutical composition comprising a compound of any one of Claims 19-25 and a pharmaceutically acceptable carrier.

20 35. A pharmaceutical composition comprising a compound of any one of Claims 26-30 and a pharmaceutically acceptable carrier.

36. The pharmaceutical composition of Claim 1, wherein said composition is administered orally.

25

37. The pharmaceutical composition of Claim 1, wherein said composition is administered parenterally.

38. A method for treating diseases related to unregulated protein kinase signal transduction comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Claim 1.

5 39. A method for treating diseases related to unregulated protein kinase signal transduction comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Claim 30.

10 40. The method of Claim 38 or 39, wherein said disease is selected from the group consisting of cancer, blood vessel proliferative disorders, fibrotic disorders, mesangial cell proliferative disorders, metabolic diseases and infectious diseases.

41. The method of Claim 40, wherein the cancer is selected from the group consisting of colorectal cancer, Kaposi's sarcoma and lung cancer.

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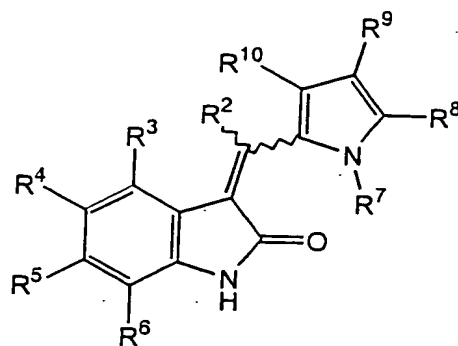
42. The method of Claim 40, wherein the blood vessel proliferative disorder is selected from the group consisting of arthritis and restenosis.

20 43. The method of Claim 40, wherein the fibrotic disorder is selected from the group consisting of hepatic cirrhosis and atherosclerosis.

25 44. The method of Claim 40, wherein the mesangial cell proliferative disorder is selected from the group consisting of glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathy syndromes, transplant rejection and glomerulopathies.

30 45. The method of Claim 40, wherein the metabolic disease is selected from the group consisting of psoriasis, diabetes mellitus, wound healing, inflammation and neurodegenerative diseases.

46. A method of synthesizing a compound of formula I comprising:  
(a) reacting a compound of the formula V:



where  $R^3$ - $R^{10}$  are as defined in Claim 1 above, with an aldehyde of the formula  $R^1\text{CHO}$  where  $R^1$  is as defined in Claim 1 above, in the presence of an organic base to provide a compound of formula I, where  $R^2$  is hydrogen.

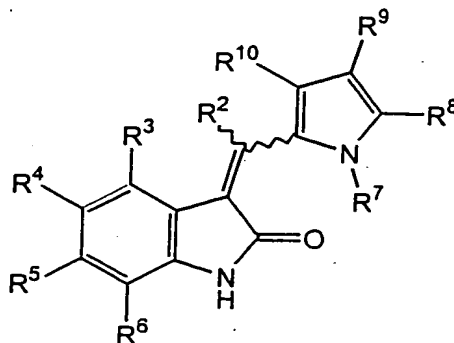
47. The method of Claim 46, further comprising reacting a compound obtained in step (a) above with an alkylating agent, an aralkylating agent, an acylating agent or a phosphorylating agent in the presence of an organic base to provide a compound of formula I where  $R^2$  is alkyl, aralkyl, aryl, acyl or  $-\text{P}(\text{O})(\text{OR})(\text{OR}')$ .

48. The method of Claim 46, further comprising removing a protecting group from the product of step (b).

49. The method of Claim 46, further comprising forming an acid addition salt.

50. A method of synthesizing a compound of formula III comprising:

(a) reacting a compound of the formula V:



where  $R^3$ - $R^{10}$  are as defined in Claim 1 above, with an acylating agent of the formula  $R^{5'}COL$ , where  $R^{5'}$  is as defined in Claim 1 above and  $L$  is a leaving group, under acylating reaction conditions in the presence of an organic base.

5

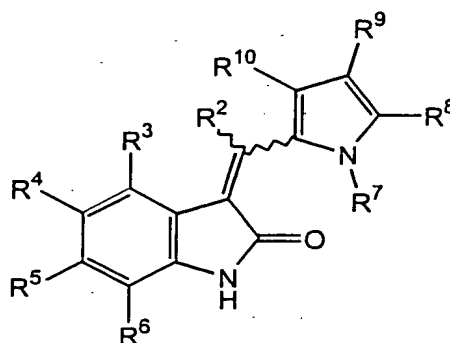
51. The method of Claim 50, further comprising removing a protecting group from the product of step (b).

52. The method of Claim 50, further comprising forming an acid addition salt.

10

53. A method of synthesizing a compound of formula IV comprising:

(a) reacting a compound of the formula V:



15 where  $R^3$ - $R^{10}$  are as defined in Claim 1 above, with a phosphorylating agent of the formula  $XP(O)(OR^a)(R^b)$  where  $R^a$  and  $R^b$  are alkyl and  $X$  is a leaving group under phosphorylating reaction conditions in the presence of an organic base.

20 54. The method of claim 53, further comprising removing the  $R^a$  and  $R^b$  groups.

55. The method of claim 53, further comprising removing a protecting group from the product of step (b).

25 56. The method of claim 53, further comprising forming an acid addition or base salt.